

## Amendments to the Specification

On page 1, after the Title of the Application, insert the following new paragraph:

### --CROSS-REFERENCE TO RELATED APPLICATIONS

Q2 This application is a U.S. National Stage application filed under 35 U.S.C. 371 of International Patent Application PCT/US00/08571 filed March 31, 2000 which in turn claims priority to U.S. provisional application 60/127,467, filed March 31, 1999.--

Please replace the paragraph beginning at page 2, lines 3-13, with the following rewritten paragraph:

Q3 --The usefulness of Antp as a vector peptide has been proven successful by genetically fusing Antp to various peptides of interest (F. Perez et al., *J Cell Sci* 102:717-722, 1992; F. Perez et al., *Mol Endocrinol* 8:1278-87, 1994; and A. Prochiantz, *Curr Opinion Neurob* 6:629-634, 1996) or by covalent linkage via cysteine residues (D. Derossi et al., *supra*). Internalization of peptides as large as 41 amino acids and of charged phosphopeptides (B. Allinquant et al., *J Cell Biol* 128:919-927, 1995) has been demonstrated in neuronal cells. In each case, the sequences fused to Antp retained their expected biological functions. Furthermore, Antp is the only translocating peptide that has been used to deliver oligonucleotides (up to 45 nucleotides in length) to cells in culture (C.M. Troy et al., *J Neuroscience* 16 253-61, 1996; G. Elliot et al., *J Virol* 72:6448-6455, 1998).--

On page 5, please delete the paragraph at lines 26-27:

~~Figures 6A and 6B show the nucleotide sequence of vector pVP22/Myc-His (SEQ ID NO:1).~~

Please replace the paragraph bridging pages 5 and 6, with the following rewritten paragraph:

CU --Figure 7 6 is a map of pVP22/Myc-His-TOPO® vector, which contains the T7 promoter (T7), VP22 open reading frame (VP22), a multiple cloning site modified by covalent coupling of the Vaccinia Virus Topoisomerase I protein (T) to linearized vector DNA, a myc epitope (*myc*), and a polyhistidine tag (6xHis). A PCR product with a single 3' A base overhang can be inserted into the topoisomerase-adapted site.--

On page 6, delete the paragraph at lines 4-5:

Figures 8A and B show the nucleotide sequence of pVP22/Myc-His-TOPO®

Please replace the paragraph bridging pages 12-13, with the following rewritten paragraph:

AS --Figure 7 6 illustrates a suitable vector wherein Vaccinia topoisomerase I linker is used to attach a translocating protein to a double-stranded oligonucleotide of interest. Vector pVP22/Myc-His TOPO® (SEQ ID NO:2), utilizes Vaccinia topoisomerase I linker to attach VP22 to a double stranded PCR product (i.e., a cell-process modifying oligonucleotide) having single 5' A base overhangs to create a VP22 fusion with vector DNA. Such topoisomerase I-DNA conjugates may then be introduced directly into cells.-

Please replace the paragraph beginning at page 13, lines 3-13, with the following rewritten paragraph:

AB --In another embodiment, a translocating protein is used to increase the efficiency of plasmid delivery in conjunction with a cationic liposome. Fusion of a translocating protein to a protein domain that readily associates with a cationic liposome, for example a hydrophobic transmembrane domain or a glycosylphosphatidylinositol (GPI) anchor, facilitates interaction at the lipid-DNA interface. Following endocytosis of the liposome-DNA complex, the translocating protein will translocate the complex through the endosomal membrane and into the cell cytoplasm and, eventually, to the nucleus for gene expression. Translocating proteins may also be used to enhance transfection efficiencies in conjunction with compounds, such as chloroquine, that inhibit lysosomal hydrolases (Niidome et al., *J. Biol. Chem.*, 272:15307-12, 1998). --

Please replace the paragraph beginning at page 28, lines 15-28, with the following rewritten paragraph:

---

an --The complete open reading frame (ORF) encoding the VP22 protein was cloned into the eukaryotic expression vector pcDNA3.1/myc-His (Invitrogen, San Diego, CA), to create the vector pVP22/*Myc*-His (Figure 5; SEQ ID NO:1), in which the ORF of the fusion partner can be inserted into a multiple cloning site located between the VP22 ORF and sequences encoding the C-terminal Anti-myc epitope and a poly His tag. The anti-myc epitope provides for easy detection of recombinant protein with Anti-myc antibody, and the poly His tag is useful for purification. Alternatively, the vector used was modified by covalent coupling of the Vaccinia Virus Topoisomerase I protein to linearized vector DNA (e.g., pVP22 TOPO® TA Cloning® Kit (Invitrogen)). In this type of vector, the ORF of a gene product of interest (i.e., a "fusion partner") was cloned as a PCR product into the vector. An example of such a Topoisomerase-adapted vector encoding the VP22 polypeptide is pVP22/*Myc*-His TOPO® vector (Figure-7 6; SEQ ID NO:2). In either case, the plasmid containing the VP22 gene fusion was then transfected into cells in culture.--

---

### Amendments To The Drawings

Applicant respectfully requests approval of amendments to the drawings as described hereafter:

Ten sheets of Drawings were in the International Application upon which the present U.S. application under 35 U.S.C. § 371 is based. Sheets 6, 7, 9 and 10 (Labeled Figures 6A, 6B, 8A and 8B) were nucleotide sequences. These original figures are now redundant over the sequence listing that has been filed in this case. Applicant respectfully requests that original drawing sheets 6, 7, 9, and 10 be cancelled.

Drawing sheet 2 has been amended to properly indicate each of Figures 2A-2D.

Drawing Sheet 3 has been amended to improve its legibility and to correct margins. The sheet has also been amended to properly label each of Figures 3A-3D.

Consistent with the cancellation of Figures 6A and 6B, the drawing originally labeled as Figure 7 (drawing sheet 8) has been relabeled Figure 6.

The remaining sheets of drawing have been formalized.

The text of the specification has been amended to be consistent with the amendment of the drawings.

None of the amendments represent the addition of new matter.

A set of clean drawings believed to comply with the requirements listed in PTO form 948 is attached.